General

Guideline Title

Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay).

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay). London (UK): National Institute for Health and Care Excellence (NICE); 2015 Oct 7. 52 p. (Diagnostics guidance; no. 18).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The procalcitonin (PCT) tests (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay) show promise but there is currently insufficient evidence to recommend their routine adoption in the National Health Service (NHS). Further research on PCT tests is recommended for guiding decisions to:

- Stop antibiotic treatment in people with confirmed or highly suspected sepsis in the intensive care unit (ICU) or
- Start and stop antibiotic treatment in people with suspected bacterial infection presenting to the emergency department (ED)

Centres currently using PCT tests to guide these decisions are encouraged to participate in research and data collection.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Bacterial infection
- Sepsis

Guideline Category

Diagnosis

Evaluation

Technology Assessment

Clinical Specialty

Critical Care

Emergency Medicine

Family Practice

Infectious Diseases

Internal Medicine

Pathology

Intended Users

Advanced Practice Nurses

Clinical Laboratory Personnel

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of using procalcitonin (PCT) testing with standard clinical practice to guide antibiotic treatment

Target Population

- People with confirmed or highly suspected sepsis in intensive care unit (ICU)
- People with suspected bacterial infection presenting to the emergency department (ED)

Interventions and Practices Considered

Procalcitonin (PCT) testing: ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay

Major Outcomes Considered

- Clinical effectiveness
  - Antibiotic exposure (initiation or duration of antibiotic therapy)
  - Resource use (number of hospital admissions, length of hospital or intensive care unit (ICU) stay, costs)
  - Adverse clinical outcomes (such as in-hospital mortality, condition-specific outcomes, antibiotic-related adverse events)
  - Health-related quality of life (HRQoL)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this diagnostics guidance and prepare a Diagnostics Assessment Report (DAR). The DAR for this diagnostic guidance was prepared by Kleijnen Systematic Reviews Ltd in collaboration with Erasmus University Rotterdam and Maastricht University (see the "Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Search Strategy

Development of search strategies followed the recommendations of the Centre for Reviews and Dissemination guidance for undertaking reviews in health care and the Cochrane Handbook for Diagnostic Test Accuracy Reviews. Strategies were based on procalcitonin (PCT) assays and target conditions (sepsis or bacterial infection); initial searches included a sensitive filter for randomised controlled trials (RCTs). Because initial searches identified no RCTs for the paediatric intensive care unit (ICU) population and only one RCT for the paediatric emergency department (ED) population, searches were re-run without a study design filter and limited to the paediatric population.

Candidate search terms were identified from target references, browsing database thesauri (e.g., MEDLINE, Medical Subject Headings [MeSH] and EMBASE Emtree), existing reviews identified during the rapid appraisal process and initial scoping searches. These scoping searches were used to generate test sets of target references, which informed text mining analysis of high-frequency subject indexing terms using EndNote reference management software. Strategy development involved an iterative approach testing candidate text and indexing terms across a sample of bibliographic databases, aiming to reach a satisfactory balance of sensitivity and specificity.

No restrictions on language or publication status were applied. Date restrictions were determined in consultation with clinical specialist members of the Assessment Subgroup, based on expert advice on the earliest appearance of literature of PCT diagnostic testing. Searches took into account generic and other product names for the intervention. The main EMBASE strategy for each set of searches was independently peer reviewed by a second Information Specialist, using the Canadian Agency for Drugs and Technologies in Health (CADTH) Peer Review Checklist. Search strategies were developed specifically for each database and keywords were adapted according to the configuration of each database.

See Appendix 1 of the Assessment Report (see the "Availability of Companion Documents" field) for full search strategies.

Rapid Appraisal Searches

To assess the scope and scale of the literature, and to identify candidate search terms, a rapid appraisal of the literature was conducted.

The following databases were searched for relevant studies from database inception date to June 2014:

- The Cochrane Library
- PROSPERO (Internet): up to 9.4.14 (http://www.crd.york.ac.uk/prospero/)

- National Institute for Health and Care Excellence (NICE) Guidance (Internet): up to 8 April 2014 (http://www.nice.org.uk/)
- National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (Internet): up to 8 April 2014 (http://www.hta.ac.uk/)
- US Food & Drug Administration (FDA) (Internet): up to 8 April 2014 (http://www.fda.gov)
- Guidelines International Network (G-I-N) (Internet): up to 9 April 2014 (http://www.g-i-n.net/)
- National Guideline Clearinghouse (NGC) (Internet): up to 9 April 2014 (http://www.guideline.gov/index.aspx)
- Medicines and Healthcare Products Regulatory Agency (MHRA) (Internet): up to 9 April 2014 (http://www.mhra.gov.uk/index.htm)
- The Medion Database up to 2014/5/4 (Internet): up to 9 April 2014

See the Assessment Report for information on RCT searches, paediatric population searches, searches for abstracts and poster presentations, and searches for completed and on-going trials.

Inclusion and Exclusion Criteria

Population

1. Adults and children with confirmed or highly suspected sepsis, in whom antibiotic therapy is indicated, who are being treated in ICUs
2. Adults and children presenting to the ED with suspected bacterial infection

Studies of neonates or immunosuppressed neutropenic patients on chemotherapy, immunosuppressant drugs or transplant programmes were excluded.

Intervention/Index Test

Treatment decisions based on laboratory-based PCT testing, using any of the tests currently available to the UK National Health Service (NHS) as described in Section 2.2 of the Assessment Report, in addition to standard practice (as reported in individual studies).

Point-of-care tests, which do not provide a quantitative estimate of PCT levels, were excluded.

Comparator

Treatment decisions based on standard practice (as reported in individual studies), without PCT testing.

Outcomes

Antibiotic exposure (initiation/duration of antibiotic therapy), resource use (number of hospital admissions, length of hospital/ICU stay, costs), adverse clinical outcomes (e.g., Sequential Organ Failure Assessment [SOFA] scores, in-hospital mortality, condition-specific outcomes), antibiotic-related adverse events.

Study Design

RCTs, or controlled clinical trials (CCTs) where no RCTs were available. Where no controlled trials (RCTs or CCTs) were available for a specified population, studies assessing the change in diagnostic accuracy associated with the addition of PCT testing to standard diagnostic work-up were sought. On the advice of clinical specialist members of the Assessment Subgroup, such studies were required to use adjudication of infection by independent panel as the reference standard; microbiological testing alone was not considered adequate. Studies that assessed the diagnostic accuracy of PCT testing alone, or that used culture alone as the reference standard, were excluded.

Inclusion Screening

Two reviewers independently screened the titles and abstracts of all reports identified by searches and any discrepancies were discussed and resolved by consensus. Full copies of all studies deemed potentially relevant were obtained and the same two reviewers independently assessed these for inclusion; any disagreements were resolved by consensus. Details of studies excluded at the full paper screening stage are presented in Appendix 5 of the Assessment Report (see the "Availability of Companion Documents" field).

The principal investigators of completed trials (identified through searches of clinical trials registries) that appeared to meet the inclusion criteria but for which no publication was identified, were contacted and asked to provide publication details or un-published data. Details of ongoing trials and trials for which data were requested are reported in Appendix 2 of the Assessment Report.

Results of the Clinical Effectiveness Assessment

The initial literature searches of bibliographic databases for RCTs identified 2,919 references. After initial screening of titles and abstracts, 146 were considered to be potentially relevant and ordered for full paper screening; of these 35 were included in the review. Additional searches of bibliographic databases for non-RCTs conducted in paediatric populations yielded an additional 515 references. After initial screening of titles and abstracts, 14 were considered to be potentially relevant and ordered for full paper screening; none of these met the criteria for inclusion in the review (see Appendix 5 of the Assessment Report). All potentially relevant studies cited in documents supplied by the test manufacturers had already been identified by bibliographic database searches. One additional publication was obtained through contact with the authors, after searches had identified the study protocol. Figure 1 in the Assessment Report shows the flow of studies through the review process, and Appendix 4 in the Assessment Report provides details, with reasons for exclusions, of all publications excluded at the full paper screening stage.

Assessment of Cost-effectiveness

Review of Economic Analyses of Procalcitonin (PCT) Assays

Search Strategy

Searches were undertaken to locate relevant economic evaluations on adults and children presenting to or being treated at EDs and ICUs with sepsis or bacterial infection.

Economic Evaluations

The following databases were searched for relevant studies from 2005 to August 2014:

- NHS Economic Evaluation Database (NHS EED) (Wiley): 2005 – Issue 3 of 4, July 2014
- Health Economic Evaluation Database (HEED) (Wiley): 2005 – 20 August 2014 (http://onlinelibrary.wiley.com/book/10.1002/9780470510933)
- IDEAS via Research Papers in Economics (RePEc) (Internet): 2005 – 20 August 2014 (http://repec.org/)
- EconLIT (EBSCO): 2005 – 20 August 2014

Inclusion Criteria

Studies reporting a full economic analysis, with (at least) one of the comparators including PCT testing and with survival and/or quality-adjusted life years (QALYs) as an outcome measure, were eligible for inclusion.

Results

The literature search identified 221 records from bibliographic database searches and supplementary searching (e.g., reference/citation checking, additional database searches including the database search for the assessment of clinical effectiveness). The studies identified through supplementary searching also included one potentially relevant unpublished paper sent by bioMérieux. After title and abstract screening, 21 records were considered to be potentially relevant and after full text screening two studies (three publications) were considered eligible for inclusion (see Figure 21 of the Assessment Report for the flow of studies for the review of economic analyses). One study considered PCT testing for adult patients with acute respiratory tract infections (outpatient setting) and one considered PCT testing for adult patients with community-acquired pneumonia (in-hospital setting). These studies are summarised in Table 8 of the Assessment Report.

Review of Health-related Quality of Life (HRQoL) Studies

Search Strategy

Searches were undertaken to locate relevant utility value studies on adults and children presenting to or being treated at EDs and ICUs with sepsis or bacterial infection.

Utility Values

The following databases were searched for relevant studies from database inception date to September 2014:

- MEDLINE (OvidSP): 1946 - August Week 3 2014
- MEDLINE In-Process Citations and Daily Update (OvidSP): up to 2 September 2014
- EMBASE (OvidSP): 1974 to 2 September 2014
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley): up to Issue 8 of 12, August 2014
- Health Technology Assessment (HTA) Database (Wiley): up to Issue 3 of 4, July 2014

- PubMed (http://www.ncbi.nlm.nih.gov/pubmed): up to 3 September 2014
- PROQOLID (Internet) (http://www.proqolid.org/): up to 3 September 2014

Inclusion Criteria

Studies reporting on HRQoL, in terms of utility scores, for patients with confirmed/highly suspected sepsis in intensive care settings or patients presenting to the ED with suspected bacterial infection were eligible for inclusion.

Results

The literature search identified 476 records (472 through database searches and four through supplementary searching). After title and abstract screening, 82 potentially relevant records were identified and after full text screening nine studies (10 papers) were considered eligible for inclusion (see Figure 22 of the Assessment Report). The HRQoL studies are summarised in Appendix 6 of the Assessment Report.

Number of Source Documents

Assessment of Clinical Effectiveness

Eighteen studies (36 publications) were included in the review.

- Studies of intensive care unit (ICU) population: Adults, n = 8 studies (15 publications); children, n = 0 studies
- Studies of emergency department (ED) population: Adults, n = 8 studies (17 publications); children, n = 2 studies (4 publications)

See Figure 1 of the Assessment Report (see the "Availability of Companion Documents" field) for the flow of studies through the review process.

Assessment of Cost-effectiveness

- Review of economic analyses of procalcitonin (PCT) assays: Two studies (three publications) were considered eligible for inclusion.
- Review of health-related quality of life studies: Nine studies (10 papers) were included.
- An economic model was submitted.

See Figures 21 and 22 of the Assessment Report for the flow of studies through the review process.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this diagnostics guidance and prepare a Diagnostics Assessment Report (DAR). The DAR for this diagnostic guidance was prepared by Kleijnen Systematic Reviews Ltd in collaboration with Erasmus University Rotterdam and Maastricht University (see the "Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Data Extraction

Data were extracted on the following: setting (intensive care unit [ICU] or emergency department [ED]); age group (adults or children); study details; inclusion and exclusion criteria; participant characteristics (demographic characteristics, primary presentation and co-morbidities); details of the procalcitonin (PCT) assay used; details of the intervention PCT algorithm (decision thresholds for PCT levels and any clinical criteria); details of the standard care comparator; outcome measures (measures of antibiotic exposure [e.g., initiation and/or duration of antibiotics]), resource use (e.g., duration of hospital stay, duration of ICU stay, secondary presentations) and adverse clinical outcomes (e.g., mortality, relapse/re-infection, Sequential Organ Failure Assessment [SOFA] score). Data were extracted by one reviewer, using a piloted, standard data extraction form and checked by a second; any disagreements were resolved by consensus. One Chinese language paper was extracted by a reviewer in consultation with a native speaker. Full data extraction tables are provided in Appendix 3 of the DAR document.

Quality Assessment

The methodological quality of included RCTs was assessed using the Cochrane Risk of Bias Tool. Risk of bias assessments were undertaken by one reviewer and checked by a second reviewer; any disagreements were resolved by consensus or discussion with a third reviewer. No studies of other designs were included in the review. The results of the risk of bias assessments are summarised and presented in tables and graphs in the results of the systematic review (see Section 3.2.2 of the Assessment Report) and are presented in full, by study, in Appendix 4 of the Assessment Report.

Methods of Analysis/Synthesis

The results of studies included in this review are summarised by population/setting, i.e., studies providing information on the effectiveness of adding PCT testing to the information used to guide antibiotic therapy for the treatment of confirmed or highly suspected sepsis in ICU settings, and studies providing information on the effectiveness of adding PCT testing to the information used to guide antibiotic therapy in people presenting to the ED with suspected bacterial infections. Within each setting, studies on adults and children are described separately. In addition, results are structured to illustrate the effects of PCT algorithms on antibiotic exposure, resource use and costs and adverse clinical outcomes.

Where more than one study reported the same outcome measure for clinically similar populations, meta-analysis was used to calculate summary effect estimates (relative risk [RR] for dichotomous outcomes and weighted mean difference [WMD] for continuous outcomes) together with 95% confidence intervals [CIs], using DerSimonian and Laird random effects models. Forest plots are used to display results from individual studies and summary estimates to allow visual assessment of heterogeneity. Heterogeneity was assessed statistically using the I^2 statistic. Observed heterogeneity was explored using subgroup analyses.

See Section 3 of the Assessment Report for additional information on clinical effectiveness analysis.

Assessment of Cost-effectiveness

Quality Assessment of the Included Studies

Review of Economic Analyses of PCT Assays

The two included studies were appraised using a quality checklist based on Drummond et al. The results of the quality assessment are shown in Table 9 of the Assessment Report (see the "Availability of Companion Documents" field).

Review of Health-related Quality of Life Studies

See Appendix 6 of the Assessment Report for details of quality assessment.

Model Structure

In a *de novo* health economic analysis (in Microsoft Excel), in accordance with the published protocol for this assessment (PROSPERO registration number CRD42014010822), PCT testing in addition to current clinical practice was compared with current clinical practice without PCT testing for: (a) adults with confirmed or highly suspected sepsis in an ICU setting (b) adults with suspected bacterial infection presenting to the ED; (c) children with suspected bacterial infection presenting to the ED. Children with confirmed or highly suspected sepsis in an ICU setting were not considered due to the lack of data.

As shown in Figures 23 and 24 of the Assessment Report, the structure of the decision tree starts with one decision node that denotes the use of PCT or current clinical practice without PCT. The key endpoints are: (i) alive with antibiotic related complications, (ii) alive without antibiotic

related complications and (iii) death. It is important to notice that treatment initiation was only explicitly incorporated in the ED setting (see Figure 24 of the Assessment Report). This is because PCT testing is mainly expected to be used to discontinue antibiotic therapy in the ICU setting (all patients with sepsis in the ICU are treated with antibiotics) whereas, in the ED setting, it is expected to be used to initiate antibiotics. What this means for parameter estimation is that, for the ED setting only, parameters are required to estimate both the probability of initiation and the duration of antibiotic use *conditional* on initiation. For the ICU setting, parameters for duration of antibiotic use only are required.

The time horizon is six months (183 days), divided into an initial short-term (28 days) phase and a subsequent phase lasting 155 days (see Figures 23 and 24 of the Assessment Report). The six months' time horizon and the initial phase of 28 days were adopted to be consistent with the outcomes reported in the studies identified in section 3 of the Assessment Report. The mean expected costs, life years (LYs), duration of antibiotic treatment and quality-adjusted life years (QALYs) are calculated separately for both strategies.

See Section 4 of the Assessment Report (see the "Availability of Companion Documents" field) for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Developing Recommendations

After reviewing the evidence the Diagnostics Advisory Committee (DAC) agrees draft recommendations on the use of the technology in the National Health Service (NHS) in England. When formulating these recommendations, the Committee has discretion to consider those factors it believes are most appropriate to the evaluation. In doing so, the Committee has regard to any relevant provisions of the National Institute for Health and Care Excellence's (NICE's) Directions, set out by the Secretary of State for Health, and legislation on human rights, discrimination and equality. In undertaking evaluations of healthcare technologies, NICE takes into account the broad balance of clinical benefits and costs, the degree of clinical need of patients under consideration, any guidance issued to the NHS by the Secretary of State that is specifically drawn to the attention of NICE by the Secretary of State, and any guidance issued by the Secretary of State, and the potential for long-term benefits to the NHS of innovation.

The Committee takes into account advice from NICE on the approach it should take to making scientific and social value judgements. Advice on social value judgements is informed in part by the work of NICE's Citizens Council.

The Committee takes into account how its judgements have a bearing on distributive justice or legal requirements in relation to human rights, discrimination and equality. Such characteristics include, but are not confined to: race, gender, disability, religion or belief, sexual orientation, gender reassignment and pregnancy or maternity.

The Committee considers the application of other Board-approved NICE methods policies, such as the supplementary guidance on discounting and the end-of-life criteria, if they are relevant to the evaluation.

Because the Programme often evaluates new technologies that have a thin evidence base, in formulating its recommendations the Committee balances the quality and quantity of evidence with the expected value of the technology to the NHS and the public.

The credibility of the guidance produced by NICE depends on the transparency of the DAC's decision-making process. It is crucial that the DAC's decisions are explained clearly, and that the contributions of registered stakeholders and the views of members of the public are considered. The reasoning behind the Committee's recommendations is explained, with reference to the factors that have been taken into account.

The language and style used in the documents produced by the Committee are governed by the following principles:

- Clarity is essential in explaining how the DAC has come to its conclusions.
- The text of the documents does not need to reiterate all the factual information that can be found in the information published alongside the guidance. This needs careful judgement so that enough information and justification is given in the recommendations to enable the reader to understand what evidence the DAC considered and, if appropriate, who provided that evidence.

The Committee may take into account factors that may provide benefits to the NHS or the population, such as patient convenience. It may also consider costs and other positive or negative impacts on the NHS that may not be captured in the reference-case cost analysis, such as improved

processes.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Base-case Analysis

Base-case analyses indicate that procalcitonin (PCT) testing with standard clinical practice dominates standard clinical practice alone for all populations, that is, it was both cost saving and more effective.

The cost savings ranged from £368 for children with suspected bacterial infection presenting to the emergency department (ED) (lower clinical extreme) to £3268 for adults with confirmed or highly-suspected sepsis in an intensive care unit (ICU) setting (lower clinical extreme).

Analysis of Alternative Scenarios

Various scenario analyses were performed to assess the impact of assumptions on the estimated outcomes (see Section 5.68 of the original guideline document).

The scenario analyses that assumed no difference in hospital stay had a substantial impact on all populations and settings. Treatment based on PCT testing with standard clinical practice became more costly (incremental costs varied between £7 for adults in the ICU and £25 for children in the ED) and remained more effective (quality-adjusted life year [QALY] gain varied between less than 0.001 for children in the ED and 0.007 for adults in the ICU) compared with standard clinical practice alone. For children presenting to the ED with suspected bacterial infection, this resulted in incremental cost-effectiveness ratios (ICERs) of £287,076 per QALY gained for the lower clinical extreme and £35,219 per QALY gained for the higher clinical extreme. For adults in both settings (and both clinical extremes), ICERs varied between £3390 and £3948 per QALY gained.

None of the other scenario analyses resulted in substantial changes to the base-case ICERs, and use of PCT testing with standard clinical practice remained cost effective compared with standard clinical practice alone.

One-way Sensitivity Analyses

One-way sensitivity analyses were performed for all stochastic input parameters between the 95% confidence intervals.

The one-way sensitivity analysis on relative mortality risk for adults with suspected bacterial infection presenting to the ED resulted in substantial changes to the base-case ICERs. Analyses showed that when using the upper bound of the 95% confidence interval (1.590; base-case value 0.850) PCT testing with standard clinical practice guided treatment was less costly (£772) and less effective (QALY loss 0.025) compared with standard clinical practice alone. This resulted in ICERs of £30,469 per QALY lost (lower clinical extreme) and £30,446 per QALY lost (higher clinical extreme).

None of the other one-way sensitivity analyses resulted in substantial changes to the base-case ICERs, and use of PCT testing with standard clinical practice remained cost effective compared with standard clinical practice alone.

Considerations

The Committee considered the cost-effectiveness of adding PCT testing to standard clinical practice in ICU settings and in the ED. It noted that in all scenarios assessed, PCT testing with standard clinical practice dominated standard clinical practice alone, that is, it was more effective and less costly. However, the Committee acknowledged that the change in QALYs was extremely small. The Committee noted its earlier conclusion that the use of PCT testing with standard clinical practice is unlikely to result in worse clinical outcomes compared with standard clinical practice alone. It therefore concluded that the QALYs for each group could be considered broadly equal, that is, adding PCT testing to standard care does not result in a meaningful change in QALYs.

The Committee considered whether the cost savings generated through reductions in resource use were large enough to offset the additional cost of PCT testing. It noted its earlier conclusion about the uncertainty of whether the reductions in resource use reported in the studies included in the systematic review would be realised in clinical practice in the National Health Service (NHS). The Committee therefore concluded that it was uncertain whether savings would be large enough in a UK setting to offset the cost of PCT testing.

See Sections 5 and 6 of the original guideline document for additional discussion of the economic analysis.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

The National Institute for Health and Care Excellence (NICE) sends the Diagnostics Assessment Report (DAR), with any confidential material removed, to registered stakeholders for comment. Stakeholders have 10 working days to return comments. Models supporting the DAR are made available to registered stakeholders on request during this period.

NICE presents anonymised registered stakeholder comments on the DAR, along with any responses from NICE or the External Assessment Group (EAG), to the Committee and later publishes these comments on its Web site.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Diagnostics Advisory Committee (DAC) considered a systematic review and an economic model prepared by an External Assessment Group.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Rapid and accurate determination of the presence or absence of bacterial infection is important to guide appropriate antibiotic therapy and to reduce unnecessary exposure to antibiotics.

Potential Harms

The Committee noted that some test results will be false positives and may influence clinical judgement resulting in people having antibiotics unnecessarily.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) will support this guidance through a range of activities to promote the recommendations for further research. The research proposed (see Section 7 of the original guideline document) will be considered by the NICE Medical Technologies Evaluation Programme research facilitation team for the development of specific research study protocols as appropriate. NICE will also incorporate the research recommendations in Section 7 of the original guideline document into its guidance research recommendations database (available on the NICE Web site) and highlight these recommendations to public research bodies.

Implementation Tools

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay). London (UK): National Institute for Health and Care Excellence (NICE); 2015 Oct 7. 52 p. (Diagnostics guidance; no. 18).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Oct 7

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Diagnostics Advisory Committee

Composition of Group That Authored the Guideline

Standing Committee Members: Professor Adrian Newland (*Chair, Diagnostics Advisory Committee*); Dr Mark Kroese (*Vice Chair, Diagnostics Advisory Committee*), Consultant in Public Health Medicine, PHG Foundation, Cambridge and UK Genetic Testing Network; Professor Ron Akehurst, Professor in Health Economics, School of Health and Related Research, University of Sheffield; Dr Phil Chambers, Research Fellow, Leeds Institute of Cancer and Pathology, University of Leeds; Professor Paul Collinson, Consultant Chemical Pathologist and Professor of Cardiovascular Biomarkers, St George's Hospital, St George's University Hospitals NHS Foundation Trust; Dr Sue Crawford, GP Principal, Chillington Health Centre; Professor Erika Denton, National Clinical Director for Diagnostics, NHS England and Honorary Professor of Radiology, University of East Anglia and Norfolk and Norwich University Hospitals NHS Foundation Trust; Dr Steve Edwards, Head of Health Technology Assessment, BMJ Evidence Centre; Mr David Evans, Lay member; Dr Simon Fleming, Consultant in Clinical Biochemistry and Metabolic Medicine, Royal Cornwall Hospitals NHS Trust; Mr John Hitchman, Lay member; Professor Chris Hyde, Professor of Public Health and Clinical Epidemiology, Peninsula Technology Assessment Group; Mr Matthew Lowry, Director of Finance and Infrastructure, Doncaster and Bassetlaw Hospitals NHS Foundation Trust; Dr Michael Messenger, Deputy Director and Scientific Manager, National Institute for Health Research Diagnostic Evidence Co-operative, Leeds; Dr Peter Naylor, GP, Chair Wirral Clinical Commissioning Group; Dr Dermot Neely, Consultant in Clinical Biochemistry and Metabolic Medicine, Newcastle upon Tyne Hospitals NHS Foundation Trust; Dr Gail Norbury, Consultant Clinical Scientist, Guy's and St Thomas' NHS Foundation Trust; Dr Simon Richards, Vice President Regulatory Affairs, EME, Alere Inc.; Dr Deirdre Ryan, Consultant Cellular Pathologist, Royal London Hospital, Barts Health NHS Trust; Dr Steve Thomas, Consultant Vascular and Cardiac Radiologist, Sheffield Teaching Hospitals NHS Foundation Trust; Mr Paul Weinberger, Chief Executive Officer, DiaSolve Ltd, London; Professor Anthony Wierzbicki, Consultant in Metabolic Medicine and Chemical Pathology, Guy's and St Thomas' NHS Foundation Trust

Specialist Committee Members: Dr John Butler, Consultant in Emergency and Critical Care Medicine, Central Manchester University Hospitals NHS Foundation Trust; Professor Enitan Carrol, Consultant in Paediatric Infectious Diseases, Alder Hey Children's NHS Foundation Trust; Dr Chris Chaloner, Consultant in Laboratory Medicine (Paediatric Biochemistry), Central Manchester University Hospitals NHS Foundation Trust; Dr Paul Dark, Consultant Intensive Care Medicine, Salford Royal NHS Foundation Trust; Dr Jim Gray, Consultant Microbiologist, Birmingham Children's Hospital NHS Foundation Trust; Miss Stevie-Louise McGuiness, Lay member; Dr Marcus Peck, Consultant in Anaesthesia and Intensive Care Medicine, Frimley NHS Foundation Trust; Dr Bob Phillips, Senior Clinical Academic and Honorary Consultant in Paediatric and Adolescent Oncology, Leeds, Teaching Hospitals NHS Trust; Mr Suman Shrestha, Advanced Critical Care Nurse Practitioner, Frimley NHS Foundation Trust

Financial Disclosures/Conflicts of Interest

Committee members are required to submit a declaration of interests on appointment, in every year of their tenure, and at each Committee meeting, in line with the National Institute for Health and Care Excellence's (NICE's) code of practice for declaring and dealing with conflicts of interest.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available in ePub or eBook formats from the NICE Web site.

Availability of Companion Documents

The following are available:

- Diagnostics Assessment Programme. Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay). Committee papers. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jan. 343 p. Available from the NICE Web site.
- Diagnostics Assessment Programme manual. London (UK): National Institute for Health and Care Excellence; 2011 Dec. 130 p. Available from the NICE Web site.

Patient Resources

The following is available:

- Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Oct. (Diagnostics guidance; no. 18). Available from the National Institute for Health and Care Excellence (NICE) Web site.

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